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Kari Alitalo

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EXAMINER

KAPUSHOC, STEPHEN THOMAS

ART UNIT

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/567,630	<b>Applicant(s)</b> ALITALO ET AL.	
	<b>Examiner</b> STEPHEN KAPUSHOC	<b>Art Unit</b> 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 May 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 and 79 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Disposition of Claims: Claims pending in the application are 1-15,17,21,22,25-29,31,33,34,36-38,41,46,48,52,54,55,68,70-76 and 79-85.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 17,21,22,25-29,31,33,34,36-38,41,46,48,52,54,55,68,70-76 and 80-85.

### **DETAILED ACTION**

Claims 1-15, 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 48, 52, 54, 55, 68, 70-76, and 79-85 are pending.

Claims 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 48, 52, 54, 55, 68, 70-76 and 80-85 are withdrawn from examination as detailed below.

Claims 1-15 and 79 are examined on the merits.

Please note: The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This Office Action is in reply to Applicants' correspondence of 05/14/2010.

Applicants' remarks and amendments have been fully and carefully considered but are not found to be sufficient to put the application in condition for allowance. Any new grounds of rejection presented in this Office Action are necessitated by Applicants' amendments. Any rejections or objections not reiterated herein have been withdrawn in light of the amendments to the claims or as discussed in this Office Action.

This Action is made **FINAL**.

### ***Election/Restrictions***

1. Applicants' confirmation (p.10 of the Remarks of 05/14/2010) of the telephonic election is acknowledged. Applicants have traversed the Requirement for Restriction indicating that a 'special technical feature' of the differently named groups related to the role/association of elevated Prox-1 expression in colon cancer. This is not found persuasive because, as detailed in the Office Action of 01/21/2010, the different claimed methods (i.e.: diagnostic, treatment, and compound screening methods) in fact require different methodological steps and do not share a common technical feature. With particular regard to Applicants' traversal, for example, the method of claim 48 (a compound screening method) does not require any relationship between elevated Prox-1 expression and colon cancer. Additionally, where Applicants assert that the prior art

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of Parr et al (2003) is not a teaching of prior art based on the Rule 131 Declaration, it is again noted that the Parr reference is presented as a secondary issue regarding lack of unity of the different inventions, and further, as detailed in this Office Action, Applicants' Declaration is insufficient to overcome the teachings of Parr et al as prior art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 17, 21, 22, 25-29, 31, 33, 34, 36-38, 41, 46, 48, 52, 54, 55, 68, 70-76 and 80-85 (note that new claims 80-85 are drawn to non-elected treatment and screening methods) are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/14/2010.

In response to Applicants assertion that claim 15 is a linking claim that links the inventions of Groups 1 and 2, it is noted that in fact claim 15 is not a linking claim. Claim 15 requires only administering a Prox-1 inhibitor, but claim 15 does not require that any growth of cancer is inhibited, or any cancer phenotype is alleviated. As such, the requirements of claim 15 are in fact different than the particularly claimed treatment methods in separate Group 2 as set forth in the Office Action of 01/21/2010.

### ***The Petrova Declaration under 37 CFR 1.131***

2. The Declaration filed on 05/14/2010 under 37 CFR 1.131 has been considered but is ineffective to overcome the Parr et al (2003) reference. 37 CFR 1.131 states: "Prior invention may not be established under this section in any country other than the

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United States, a NAFTA country, or a WTO member country.” In the case of the instant Declaration, part 2 recites only “work we had performed in our laboratory”, but there is not statement regarding the country in which the work was performed and the invention was made.

As such, the rejections of claims under 35 USC 102 and 103, as anticipated and obvious in view of the teachings of the prior art, as set forth in the Office Action of 01/21/2010, are **MAINTAINED** in this Office Action.

### ***Maintained Claim Objections***

3. Claims 1, 11 and 13 are objected to because of the following informalities: Claims 1, 11, and 13 recite the gene symbols Prox-1 (claim 1), CD44, Enc1, and ID2 (claim 11) and APC (claim 13), where at the first instance of each gene symbol in the claims the symbol should be accompanied by the full gene name. For example, in claim 1, “measuring Prox-1 (prospero homeobox protein 1) expression or activity”. Appropriate correction is required.

### ***Maintained Claim Rejections - 35 USC § 112 2<sup>nd</sup> ¶ - Indefiniteness***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:
- The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 1-15 and 79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-15 and 79 are unclear over the stated purpose of the claimed methods as "screening colon tissue for colon cancer" as stated in the preamble of claim 1. Claim 1 recites "wherein elevated Prox-1 expression or activity in the colon tissue correlates with the presence of colon cancer", however there is no required method step where an "elevated Prox-1 expression or activity" is in fact detected. As such there is not a nexus between the recited purpose of the claimed method, the 'wherein clause', and the required method steps, and as such it is unclear how the performed method steps accomplish the stated purpose of the claimed method.

### **Response to Remarks**

Applicants have traversed the rejection of claims under 35 USC 112 2<sup>nd</sup> paragraph as indefinite. Applicants arguments (p.11 of Remarks), and the amendments to the claims, have been fully and carefully considered but are not found to be persuasive to withdraw the rejection. Applicants have argued that the amended claims require 'screening for colon cancer from the measuring of the Prox-1 expression or activity' and that a screening method can provide valuable information where no elevation of Prox-1 is detected. The argument is not persuasive. Initially, a method wherein no Prox-1 elevation is detected is not consonant with the 'wherein' clause, which, as stated in the rejection, appears to require elevated expression. Further, in view of Applicants argument, it appears that applicants are claiming a method where the only step is measuring Prox-1 expression and activity and, according to the arguments, detecting any level (increased, decreased, elevated, non-elevated) of expression or activity. Thus it would appear from applicants arguments that, with regard for example

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to independent claim 1, the only differentiation between the claimed 'method of screening' and any prior art wherein Prox-1 expression or activity was measured in colon tissue from a mammal, is the recitation of the preamble, and the step 'screening for colon cancer from the measuring of the Prox-1 expression or activity', where there are no clearly required steps of any such 'screening from the measuring step'.

The rejection is **MAINTAINED**.

***Withdrawn Claim Rejections - 35 USC § 112 2<sup>nd</sup> ¶ - Indefiniteness***

The rejection of claims 11-13 under 35 USC 112 2<sup>nd</sup> paragraph, as set forth on page 6-7 of the Office Action of 01/21/2010, is **WITHDRAWN** in light of the amendments to the claims.

***Maintained Claim Rejections - 35 USC § 112 1<sup>st</sup> ¶ - Scope of Enablement***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-15 and 79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for determining an increased likelihood of the presence of colon cancer in a human subject suspected of having colon cancer, said method comprising:

obtaining a sample of colon tissue from said subject;  
detecting an abundance of prox-1 (prospero homeobox protein 1) mRNA in said sample that is indicative of an elevated level of prox-1 expression, wherein said elevated level is statistically significantly



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increased as compared to the level of prox-1 expression in a population of colon tissue samples that do not have cancer; and  
correlating the presence of said elevated level of prox-1 expression in said sample with an increased likelihood of the presence of colon cancer in the subject

does not reasonably provide enablement for the methods as claimed which encompass any level of elevated expression or activity, diagnosis of any pathological condition in a colon tissue, analyses performed in any mammal, and detection of any analyte to measure prox-1 expression. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

**Nature of the invention and breadth of the claims**

The claims are drawn to methods for detecting a pathological condition in colon tissue comprising analysis of prox-1 expression.

The claims encompass the detection of any level of elevated gene expression as compared to any level.

The claims encompass the detection of any pathological condition in any subject mammal.

The claims encompass the analysis of analyte for the determination of elevated gene expression.

The claims thus require knowledge of a correlation between any level of elevated gene expression according to any measured analyte, in any subject organism and the presence of any pathological condition.

**Direction provided by the specification and working example**

The instant specification provides an analysis of prox-1 mRNA expression in human colon cancer samples as compared to other tumor types and non-tumor controls. The specification teaches that prox-1 is significantly increased in colon tumor samples as compared to non-cancer tissue (p.60 - Example 2). The instant specification does not provide any example of any pathological condition other than colon cancer tissue analysis.

The instant specification does not provide for any statistical or quantitative analysis of the expression of prox-1 protein in tissue samples (p.60-61) and teaches that some tumor samples did not show increased protein expression. The instant specification asserts that studies may be performed to measure if prox-1 protein correlates with prox-1 mRNA (p.75-76 – Example 11), but does not provide any evidence that such a correlation exists, or that prox-1 protein expression is diagnostically indicative of any colon pathology.

**State of the art, level of skill in the art, and level of unpredictability**

While the state of the art and level of skill in the art with regard to the analysis of gene expression in any sample is high, the unpredictability in associating any gene expression level with an condition, as generically encompassed by the claims, is higher.

Because the claims encompass the analysis of gene expression in any mammal, whereas the specification teaches only the statistical analysis of human samples, it is relevant to point out the unpredictability in extrapolating gene expression results among different organisms. For example, Hoshikawa et al (2003) teaches unpredictability with regard to applying gene expression results among different organisms. The reference

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teaches the analysis of gene expression in lung tissue in response to hypoxic conditions which lead to pulmonary hypertension (Fig. 1). The reference teaches that the gene expression profile in mouse is different from that observed in rat (Tables 1-4; p.209 - Abstract). Thus it is unpredictable as to whether or not any genes that are colon cancer-related in, for example, humans are in fact applicable to diagnosing any different pathological condition in any other non-human organism.

Because the claims encompass detecting any level of gene expression in a sample from an individual and comparing that level to any control level or average level to determine an elevated level that is indicative of rejection, it is relevant to point out the unpredictability associated with gene expression in any individual. Cheung et al (2003) teaches that there is natural variation in gene expression among different individuals. The reference teaches an assessment of natural variation of gene expression in lymphoblastoid cells in humans, and analyzes the variation of expression data among individuals and within individuals (replicates) (p.422, last paragraph; Fig 1). The data indicates that, for example, expression of ACTG2 in 35 individuals varied by a factor of 17; and that in expression of the 40 genes with the highest variance ratios, the highest and lowest values differed by a factor of 2.4 or greater (Fig 3). Similarly, the prior art of Shalon et al (2001) teaches that preferably 20-50 different test individuals are assayed to obtain meaningful data showing a significant change in gene expression levels, and changes of gene expression of at least 2 fold and up to 100 fold or more are desirable for the comparison of gene expression levels between a case and control population (p.10 ¶156, ¶158).

And while the claims encompass any analyte in the measure of gene expression (e.g.: activity, or protein levels), while the specification teaches only the significant association of mRNA levels with the presence of colon cancer, it is relevant to point out that other measure of gene expression do not always correlate with mRNA levels. For example, Chen et al (2002) teaches that it is typical for protein abundances to not be correlated with mRNA abundances in tissue samples. It is thus unpredictable as to whether or not any non-mRNA analyte would in fact be predicative of mRNA expression.

#### **Quantity of experimentation required**

A large and prohibitive amount of experimentation would be required to make and use the claimed invention. Such experimentation would require case:control analysis of prox-1 gene expression from any organism of interest. Such experimentation would further require the analysis of different types of analytes and potential correlations with any pathological condition. Even if such experimentation were to be performed, there is no assurance that the any associations beyond those identified in the specification (i.e. elevated prox-1 mRNA expression in colon tissue as indicative of likelihood of colon cancer in humans) would be confirmed.

#### **Conclusion**

Taking into consideration the factors outlined above, including the nature of the invention and breadth of the claims, the state of the art, the level of skill in the art and its high level of unpredictability, the lack of guidance by the applicant and the particular examples, it is the conclusion that an undue amount of experimentation would be

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required to make and use the claimed invention in the full scope as encompassed by the claims.

### **Response to Remarks**

Applicants have traversed the rejection of claims under 35 USC 112 1st paragraph for encompassing non-enabled scope. Applicants' arguments (p.12-13 of Remarks) have been fully and carefully considered but are not persuasive to withdraw the rejection.

Applicants have argued, in response to the indication in the rejection that an enabled method requires detection of a statistically significant increased amount of Prox-1 mRNA, that the specification enables measurements that are not scored as elevated. The Examiner maintains that in so far as a method for screening for colon cancer has the goal of detecting the presence of cancer, the instant specification demonstrates that prox-1 mRNA overexpression is present in colon cancer samples. With regard to detecting significantly elevated levels, where Applicants argue that the skilled artisan could measure a level of an analyte and draw a conclusion as to the presence or absence of cancer, the Examiner maintains that such an argument disregards the teachings of the instant specification (demonstrating significant overexpression of prox-1 mRNA in colon cancer as compared to non-cancerous colon tissue) in view of the cited Cheung reference (which teaches that there is broad variation in gene expression measured even between very similar individuals). Thus while methods for determining the significance of any differences in gene expression are known in the art, the instantly claimed methods are not drawn to gene expression

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analysis methods per se, but the use of measured gene expression in a diagnostic method.

Applicants have further argued that the instant specification is fully enabled for the breadth of 'prox-1 expression of activity' (i.e.: any mRNA, protein, or activity measurement). Applicants have argued that analysis of siRNA inhibition and prox-1 related pathways is more probative than the teachings of the art cited in the rejection indicating that in fact it is common for mRNA levels and protein levels to be discordant in tissue samples. The Examiner maintains that the instant claims are drawn to methods which require drawing diagnostic conclusions (e.g. that cancer is present) based on a measured analyte, where the instant specification provides a diagnostic relationship with the measure only of mRNA and the cited art shows the unpredictability is extrapolating any diagnosis based on mRNA levels to other analyte levels. It should also be noted that the Examiner has not indicated that, in view of the teachings of the prior art, teachings regarding prox-1 mRNA in colon cancer render obvious methods particularly requiring either protein or 'activity' measurement. If Applicants have any evidence that in fact an increased level of protein, or some particular measured prox-1 activity, can be reliably and robustly associated with the presence of colon cancer, they are encouraged to provide such evidence in the form of a Declaration for reconsideration of that aspect of the instant rejection.

Finally, Applicants have asserted that prox-1 gene expression was measured in a mouse model, and as such the claims are fully enabled for any mammal. The Examiner maintains that, as established by the art cited in the rejection, differences in gene

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expression among different animals is well known to the skilled artisan. And while Example 13 of the specification deals with a genetically modified mouse model, such model are known to be quite different than naturally occurring in vivo environments. Further it is noted that even in the mouse model systems analyzed, only one of the two models analyzed supported the required association between prox-1 elevation and colon cancer.

The rejection as set forth is **MAINTAINED**.

***Maintained Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-4, 7, 9, 10, 14 and 79 are rejected under 35 U.S.C. 102(a) as being anticipated by Parr et al (2003) (this reference was publicly available as of 7/17/2003).

Parr et al teaches that elevation of prox-1 mRNA in colon tissue as compared to normal colon mucosa is indicative of the presence of colon cancer (e.g.: Fig 1 and 2; p.534 – Materials and methods; p.536 – Prox-1 and podoplanin were significantly increased in colon cancer and Prox-1 was linked with local invasion; Table III; p.538, left col. last paragraph). Thus Parr et al provides a method for screening colon tissue for a pathological condition meeting the limitations of claim 1, and teaches comprising sample tissue expression to healthy tissue (claim 2), obtaining a colon tissue sample

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(claim 3), identifying colon cancer tissue (claim 4), measuring prox-1 mRNA (claim 5), isolating mRNA (claim 9), performing QPCR (claim 10), and analysis of humans (claim 14).

Relevant to claim 79, Parr et al teaches the association of elevated prox-1 expression with colon cancer, and that the prox-1 marker offers prognostic value for colon cancer patients (e.g. p.538, left col., last paragraph), thus providing a diagnosis of colon cancer for samples wherein an elevated prox-1 expression level is detected.

***Maintained Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Parr et al (2003) (this reference was publicly available as of 7/17/2003).

Parr et al teaches that elevation of prox-1 mRNA in colon tissue as compared to normal colon mucosa is indicative of the presence of colon cancer (e.g.: Fig 1 and 2; p.534 – Materials and methods; p.536 – Prox-1 and podoplanin were significantly increased in colon cancer and Prox-1 was linked with local invasion; Table III; p.538, left col. last paragraph). Thus Parr et al provides a method for screening colon tissue for a pathological condition meeting the limitations of claim 1, from which rejected claim 15 depends.



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Parr et al does not teach a step of administering to a subject a composition comprising a prox-1 inhibitor.

However, Parr et al does teach that the over-expressed factors identified by Parr et al, such as prox-1, may represent a target for therapeutic strategies (p.538, left col. last paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered to a colon cancer subject that over expresses prox-1 a compound that inhibits prox-1. The skilled artisan would have recognized that Parr et al teaches that over expression of prox-1 is required for colon cancer development, and thus the skilled artisan would recognize that using prox-1 as a therapeutic target, as taught by Parr et al, would include use of compounds that inhibit the over expressed element.

9. Claims 8 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parr et al (2003) as applied to claim 15 above, and further in view of Rockman et al (2001).

Parr et al teaches all of the limitations of claim 1, from which rejected claims 8 and 11-13 depend.

Parr et al does not teach mRNA measurement by in situ hybridization (claim 8), analysis of ID2 expression (claim 11), or measuring B-catenin/TCF activation (claim 12) by nuclear localization of B-catenin (claim 13). However, such methods in the analysis of colon cancer were well known in the art at the time the invention was made.

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Rockman et al teaches the analysis of mRNA expression using in situ hybridization (e.g. o.45113 – In situ hybridization), the overexpression of ID2 in colon cancer cells (e.g. p.45113 – Abstract), B-catenin/TCF activation in colon cancer cells (e.g. p.45113 – Abstract), and that B-catenin/TCF activation can be indicated by nuclear localization of B-catenin (e.g. p.45115, right col., third full paragraph).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the in situ hybridization methods of Rockman et al for the analysis of prox-1 expression as taught by Parr et al. The skilled artisan would have been motivated to use the in situ hybridization methods of Rockman et al because the skilled artisan would have recognized that such methods represent alternative methods that can successfully identify gene expression levels.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used other indicators of the presence of colon cancer, such as ID2 over expression, B-catenin/TCF activation and nuclear localization of B-catenin, as taught by Rockman et al, in the colon cancer detection methods of Parr et al. The skilled artisan would have been motivated to use additional indicators of colon cancer, as taught by Rockman et al because the skilled artisan would recognize that the inclusion of additional measured parameters in a screening method would make the screening more robust and reliable.

### ***Conclusion***

10. No claim is allowed.

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Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Kapushoc whose telephone number is 571-272-3312. The examiner can normally be reached on Monday through Friday, from 8am until 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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/Stephen Kapushoc/  
Primary Examiner, Art Unit 1634